

**[84] Patient views on I-neb Insight Online – a telemedicine-based patient management system**

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I-neb Insight Online is a telemedicine-based patient management system that includes a multi-access information hub which allows the patient and clinician to access data on patient adherence to treatment, compliance with correct use and cleaning of the I-neb AAD System device.

A 13 week handling study of the I-neb Insight Online patient management system was conducted in forty-nine adult patients with cystic fibrosis (CF). At the end of the study patients were asked to complete a questionnaire regarding their views on I-neb Insight Online. We present the results from the 33 questionnaires that were returned by patients relating to the management of their treatment when using I-neb Insight Online (Table 1).

Table 1

No.	Questions related to management of their treatment.	Yes	No	Note
1	Did you find that using Insight Online meant that you used your I-neb more than previously?	9	25	One patient answered 'yes' and 'no'
2	Were you contacted by a member of the Patient Support Team (PSP) during the handling study regarding your treatment data?	30	2	
3	Was a problem identified with your treatment data?	22	9	
4	Was this something you were aware of before PSP contacted you?	18	11	
5	Did you find the Treatment View data useful?	29	5	One patient answered 'yes' and 'no'
6	Did you find the Device View data useful?	26	5	

A follow on to Q5 asked 'Please detail what you found useful about the Treatment View data'; 13 patients commented it helped them view their use of the device and 8 patients that it helped them view their treatment times. A follow on to Q6 asked 'Please detail what you found useful about the Device View data'; 12 patients commented that they thought it was useful for monitoring the performance of the mesh.

Patient opinions on using the I-neb Insight Online system were positive and showed that patients thought its use had positive benefits in a number of different aspects of their inhalation therapy management.

**[85] I-neb Insight Online – a telemedicine option in the treatment of cystic fibrosis**

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I-neb Insight Online is a telemedicine-based patient management system that facilitates the analysis and presentation of data on a patients' use of their I-neb Adaptive Aerosol Delivery (AAD) System. Patients upload treatment data from a patient logging system (PLS) contained within the I-neb AAD System to a remote server using their home computer and an internet connection. The data is analyzed and presented as summary graphs available to patients, their clinicians, and patient support program (PSP) personnel. If data falls outside expected values the patient and clinician are alerted so they can adjust the patient's treatment accordingly. A 13 week handling study was performed to assess use of the I-neb Insight Online technology in patients with cystic fibrosis (CF). Forty-nine patients were enrolled (median age 30, range 17.9–50.8 years), and 44 successfully completed the study. Patients performed 410/607 expected weekly uploads of data and prescription updates were initiated by either the patient or clinician. Sixty-five percent of treatment issues were resolved following contact between PSP personnel and the patient. Complete prescription and PLS data was available for 38 patients and showed a mean adherence of 69.4%, a mean compliance of 98.0%, a mean TBM treatment time of 4.9 min, and a mean TIM treatment time of 2.9 min over the course of the study. The I-neb Insight Online patient management system provides remote access to up-to-date adherence, compliance and device data for the identification of treatment issues in order to improve management of inhalation therapy for patients with CF.

**[86] Genome wide random screening strategy for the discovery of novel antimicrobial targets in *Pseudomonas aeruginosa***

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In the *P. aeruginosa* PAO1 genome 32% of the genes show no homology to previously reported sequences and only 6.7% have experimentally demonstrated functions. Hence, there is plenty of scope for the discovery of new antimicrobial targets within this organism. To this effect we used a genomic approach to search the entire *P. aeruginosa* genome for novel genes required for virulence. We screened a 60,000 Tn5 mutant library mutants in a *P. aeruginosa* PAO1 strain tagged with a *lecA::lux*-based transcriptional fusion reporting on the expression of the *lecA* cytotoxic lectin. All mutants were individually tested for reduced *lecA* expression, pyocyanin production, swarming and exo-protease, and for alterations in antibiotic susceptibility. A total of 273 pleiotropic mutants were further tested for attenuation in *Caenorhabditis elegans* and *Drosophila melanogaster* disease models, and for reduced cytotoxicity or inflammatory response in respiratory cell lines. Some of those showing the highest attenuation were then tested in the mouse model of acute infection. In summary, this study has identified a number of novel genes impacting on the virulence of *P. aeruginosa*, which are highly conserved across multiple sequenced genomes from this organism and which could potentially be exploited as novel antimicrobial targets.

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**[87] Degradation of fibrinogen by CF-associated pathogens**

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Haemoptysis is a common complication of advanced airway disease in cystic fibrosis (CF). The underlying cause of haemoptysis remains unclear, but studies suggest that infection plays a major role. In this study we investigated the ability of proteinases, secreted by three relevant CF pathogens, to degrade fibrinogen (FBG). Our results show that multiple proteinases secreted by *Pseudomonas aeruginosa* and *Burkholderia cenocepacia* were able to degrade FBG, and that this degradation differed from that observed when FBG was co-incubated with thrombin. Zymography results revealed that FBG degradation by proteinases from *Burkholderia multivorans* was less pronounced. In addition, we investigated the effects of various broad-spectrum and specific proteinase inhibitors on the ability of the bacterial proteinases to degrade FBG. Treatment of the bacterial supernatant-FBG co-cultures with individual inhibitors resulted in partial inhibition of degradation, indicating that degradation is likely to be due to multiple proteinase species. We then studied the effects of this degradation on the ability of FBG to form a thrombin-mediated clot. Our results show that degradation prevents the polymerisation of FBG and is therefore unable to form fibrin clots *in vitro*. We are currently assessing the impact of the bacterial samples on platelet aggregation. These assays will not only provide functional data but will assist us in identifying specific bacterial proteins/proteinases that are involved in the disruption of the clotting process. To date, our results suggest that bacterial proteinases may contribute to the haemoptysis observed in advanced CF airway disease by disrupting clot formation.